REMARKS

Claims 4-17, 29-56, and 58-61 are currently pending in this application. Claims 29-33 and 53-55 stand withdrawn. Claims 1-3, 18-28, and 57 were previously cancelled without prejudice or disclaimer as to the subject matter contained therein. Applicants respectfully reserve the right to prosecute the subject matter of the cancelled claims in one or more continuation or divisional applications. Claims 58-61 have been added. Claims 4-17, 34-52 and 56 are amended herein. Applicants have amended claim 13 to recite "protoporphyrin compound or its complexes with an iron atom" which is taught by the specification to include protoporphyrin, e.g., haeme and haemin. Specification at page 7 lines 14-16. Claims 4-17, 29-56, and 58-61 will remain pending on entry of the current amendments.

Support for the amended and new claims can be found throughout the specification as originally filed, *inter alia*, on page 6 lines 19-29, on page 7 lines 3-19, on page 8, lines 34-35, on page 12, lines 14-23 and in Example 1, Experiments 1 and 2. Accordingly, Applicants submit that no new matter is introduced by way of the present amendments.

Applicants submit that their claims, prior to the amendments in this Response were patentable for all the reasons set forth during prosecution of this application. Applicants amended their claims to expedite prosecution.

Summary of Telephonic Interviews

Applicants previously provided a summary of the telephonic interview conducted on November 11, 2005, between Mr. Stanislaus Aksman, Mr. Robert C. Lampe III, and Examiner Chih-Min Kam, Ph.D. This Summary of Telephonic Interview was provided in Applicants' RCE submission dated January 11, 2006.

On August 7, 2006, Mr. Stanislaus Aksman, Applicants' representative, and Examiner Chih-Min Kam discussed a proposed amendment of claim 13, and addition of dependent claims, substantially as the amended claim 13 and new claims 58-61 in this response. The Examiner advised that such amendments are likely to be favorably considered, but she may need to conduct a supplemental search to determine patentability of the claim(s), under 35 U.S.C. § 112, first paragraph.

Applicants and the Examiner also discussed the obviousness rejection over Kaneko *et al.*, U.S. Patent No. 5,075,226 ("Kaneko *et al.*"). Ms. Kam pointed out that Applicants' claim 13 uses the transitional phrase "comprising" and therefore may include materials other than the claimed starter culture composition, e.g., the product of Kaneko's examples which includes diacetyl and acetonin. The Examiner said that amounts of haemin used by Kaneko are the same or similar to those used in Applicants' application. Applicants pointed out that their claims recite an "isolated starter culture". The Examiner said she would take that into account when she reviews the response to the outstanding Office Action.

The Examiner indicated that she would contact Applicants in an effort to resolve issues, if any, after she reviews the Response.

Applicants express their appreciation to the Examiner for granting this telephone interview.

Rejections

Applicants appreciate the Examiner's withdrawal of certain of the previously raised rejections to the claims in the instant application.

Claims Rejections- 35 U.S.C. §112, first paragraph

Claims 4-17, 34-52, and 56 were rejected under 35 U.S.C. § 112, 1st paragraph, for the scope of enablement. More specifically, claims 4-17, 34-52 and 56 were rejected as allegedly lacking enablement for lactic acid bacterial cells modified to contain at least 0.1 ppm of any porphyrin containing compound. Claim 5 was rejected under 35 U.S.C. § 112, 1st paragraph, as allegedly lacking enablement for lactic acid bacterial cells modified when treated under anaerobic conditions. Claims 8 and 9 were rejected under 35 U.S.C. § 112, 1st paragraph, as allegedly lacking enablement for making cells that will be effective when inoculated in a concentration of 10^7 cells/ml into low pasteurized skim milk having 8 ppm of dissolved oxygen. Claim 9 was rejected under 35 U.S.C. § 112, 1st paragraph, as allegedly lacking enablement for lactic acid bacterial cells modified when treated under anaerobic conditions. Claim 12 was rejected under 35 U.S.C. § 112, 1st paragraph, as allegedly lacking enablement for lactic acid bacterial cells modified when treated under anaerobic conditions. Claim 16 was rejected under

35 U.S.C. § 112, 1st paragraph, as allegedly lacking enablement for lactic acid bacterial cells modified to contain at least 0.1 ppm of any porphyrin containing compound using pure strains. Claims 40-42 and 45-47 were rejected under 35 U.S.C. § 112, 1st paragraph, as allegedly lacking enablement for making and/or using the invention at "at least 60 ppm or higher of a porphyrin-containing compound", or "at least 40 ppm or higher of a cytochrome", respectively. Claims 48-52 were rejected under 35 U.S.C. § 112, 1st paragraph, as allegedly lacking enablement for cells otherwise treated that reduce the amount of dissolved oxygen at greater than 35% per hour.

Applicants respectfully disagree and traverse this rejection.

As an initial matter, Applicants respectfully submit that the Office Action erred by failing to articulate adequate basis for maintaining the rejection in view of the Declaration by Mr. Asger Geppel ("the Geppel Declaration"). In *In re Alton*, 76 F.3d 1168, 37 U.S.P.Q.2d 1578 (Fed. Cir. 1996), the Court of Appeals for the Federal Circuit reversed a decision of the U.S. Patent and Trademark Office Board of Patent Appeals and Interferences ("Board"), upholding a written description rejection alleging that the specification failed to provide a written description for the claimed subject matter, because the Examiner erred in mistaking a question of fact for a question of law and by failing to articulate adequate reasons to rebut a Declaration filed in response to the rejection. 37 U.S.P.Q. at 1579-1583.

In reversing the Board, the Federal Circuit held that the Examiner, "bears the initial burden...of presenting a *prima facie* case of unpatentability." *Id.* at 1583, quoting from *In re Oetiker*, 977 F.2d 1443, 1445, 24 USPQ 1443, 1444 (Fed. Cir. 1992). In the factual context of *Alton* in order to meet his burden of proof, the Examiner, "...must provide reasons why one of ordinary skill in the art would not consider the description sufficient." *Id.* Once the Examiner establishes a *prima facie* case of unpatentability, "the burden of coming forward with evidence or argument shifts to the applicant". *Id.* After evidence or argument is submitted by applicant, patentability is determined on the totality of the record by a preponderance of the evidence with due consideration to persuasiveness of the argument and evidence submitted by applicant in response to a rejection. *Id.*

During prosecution, Alton submitted a Declaration by Dr. Wall ("Wall Declaration") in response to the written description rejection, stating that one of ordinary skill in the art would have understood that the specification adequately described the claimed invention. *Id.* at 1581-82. The Examiner dismissed the Wall Declaration without an adequate explanation of how the

declaration failed to overcome the *prima facie* case. Instead, the Examiner gave little or no weight to the Wall Declaration asserting that it was inadequate because it did not, "...suggest that the written description in the specification supports an interferon-gamma analog which *must* have the claimed structure," and, "...the number of possible interferon-gamma analogs encompassed by the written description of the invention is substantial and the specification does not lead to any compound which must have the claimed structure." *Id.* at 1582; 1584.

The Federal Circuit held that "the declaration [was] offering factual evidence in an attempt to explain *why* one of ordinary skill in the art would have understood the specification to describe," the claimed invention. *Id.* at 1583 (emphasis in the original). The Federal Circuit stated that, "[t]he statement in the examiner's answer that the number of possible analogs encompassed by the specification is substantial does not rebut the thrust of the Wall declaration because the Wall declaration explains why one of ordinary skill in the art would have realized that Alton had possession of one particular analog." *Id.* at 1584. The Federal Circuit continued that, "...the examiner dismissed the Wall declaration and provided only conclusory statements as to why the declaration did not show that a person skilled in the art would realize that Alton had possession of the claimed subject matter...". The Federal Circuit concluded that "...by failing to articulate adequate reasons to rebut the Wall declaration, the examiner and Board failed to consider the totality of the record...". *Id.* at 1584. Therefore, it is an error as a matter of law to summarily dismiss a declaration without treating it on its merits.

In the Applicants' '680 Application, in the Office Action of April 19, 2005, claims 1, 4-17, 34-52 were rejected under 35 U.S.C. § 112, first paragraph, because allegedly the specification ". . . while enabling for lactic acid bacterial cells modified to contain at least 0.1 ppm haemin, does not reasonably provide enablement for lactic acid bacterial cells modified to contain at least 0.1 ppm of ***any*** **porphyrin** containing compound . . ." *See* April 19, 2005 Office Action, page 4. To overcome this rejection, Applicants submitted an Amendment and the Geppel Declaration to explain why Mr. Geppel, a person of ordinary skill in the art, opined that he would be enabled by Applicants' specification to make lactic acid bacterial ("LAB") cells ". . . comprising an iron containing porphyrin ring, when cultured in a fermentation medium containing any of the iron containing porphyrin compounds in any effective amounts desirable, without undue experimentation, if any were needed." Mr. Geppel used the term "effective amount" "to have the same meaning as in the '680 application, i.e., 'an amount that is sufficient

to cause the lactic acid bacterium to become modified', e.g., *See* page 6, lines 7-8." *See* the Geppel Declaration, paragraph 11. Mr. Geppel also stated that "Since all types of iron containing porphyrin compounds are closely related (*See* specification, page 7, lines 14-16), it is my opinion that the invention should work for all types of iron containing porphyrin compounds. Further, the specific source of the iron containing porphyrin compound added to the fermentation medium is not relevant." *Id.*, paragraph 12.

The Geppel Declaration was submitted in light of the specification's teachings of how to make and use the claimed invention using a variety of porphyrin compounds which include iron, which provided ample definition of "porphyrin compounds" including at least one example using haemin. Specification at page 7 lines 3-19; Example 1. Thus the Geppel Declaration provided an explanation to elucidate how a person of ordinary skill in the art, using the ample guidance in the specification and the well-developed art of porphyrin compounds, would have known, based on the specification in light of the art, how to practice the invention without undue experimentation.

However, the Office Action failed to address the substantive evidence presented in the Geppel Declaration. Instead the Office Action asserted that because of knowledge in the art of "numerous iron containing porphyrin compounds" with "different cellular association characteristic with different bacteria" it is "wholly unpredictable" how to "achieve the containment of at least 0.1 ppm of iron containing porphyrin compounds other than those demonstrated". Office Action at 4. These assertions were made in the absence of any evidence, references, or discussion of the merits of the Geppel Declaration. Therefore, the Office Action failed to consider whether the totality of the record establishes patentability of the Applicants' claimed invention, measured by a preponderance of the evidence with due consideration to persuasiveness of argument, and the Declaration, in light of the specification, as required by *In re Alton.*

It is well established under 35 U.S.C. §112 ¶ 1, that "[t]he test of enablement is whether one reasonably skilled in the art could make or use the invention from the disclosures in the patent coupled with information known in the art without undue experimentation." (*United States v. Telectronics, Inc.*, 857 F.2d 778, 785 (Fed. Cir. 1986)). The test of enablement is not whether any experimentation is necessary, but whether, if experimentation is necessary, it is undue. *In re Angstadt*, 537 F.2d 498, 504, 190 USPQ 214, 219 (CCPA 1976), MPEP § 2164.01.

There is no requirement for a reduction to practice for each embodiment of the claims because an applicant need not have actually reduced the invention to practice prior to filing. In *Gould v. Quigg*, 822 F.2d 1074, 1078, 3 USPQ 2d 1302, 1304 (Fed. Cir. 1987), as of Gould's filing date, no person had built a light amplifier or measured a population inversion in a gas discharge. The Federal Court held that "The mere fact that something has not previously been done clearly is not, in itself, a sufficient basis for rejecting all applications purporting to disclose how to do it." 822 F.2d at 1078, 3 USPQ2d at 1304. Here, Mr. Aspger Geppel in his Declaration opines that based on the totality of the specification including the working example with haemin, a person of ordinary skill in the art would be able to use any iron-containing porphyrin compound to make LAB cells as defined by the claims without undue experimentation. See Declaration at ¶ 11.

Moreover, if the invention is disclosed in such manner that one skilled in the art will be able to practice it without undue experimentation the specification does not need to contain an example at all. *In re Borkowski*, 422 F.2d 904, 908, 164 USPQ 642, 645 (CCPA 1970). Only an enabling disclosure is required. And, in particular, the lack of a working example is usually a factor considered most relevant to cases involving an unpredictable and undeveloped art.

Here, as discussed in the Declaration all iron containing porphyrin compounds (iron complexed forms) are closely related. And in the opinion of Asger Geppel, a person of ordinary skill in this technology, a person of ordinary skill understands that all iron containing porphyrin compounds share the same chemical core structure. Declaration at ¶ 14. Therefore, the teaching in the Applicants' example, using heamin, in view of the specification, would translate to similar iron containing porphyrin compounds because a person skilled in the art would understand that iron containing porphyrin compounds are functionally and structurally related. Declaration at ¶14.

Applicants note that following entry of the amendments presented herein, claims 4 and 13 will be independent claims. Applicants submit that claims 4 and 13, and the claims depending therefrom, are enabled for their full scope for the reasons set forth in greater detail below.

Applicants submit that the skilled artisan is enabled to make and use the claimed invention without undue experimentation. For example, claim 13 has been amended herein to recite that the modified lactic acid bacterial cell comprises at least 0.1 ppm on a dry matter basis of a protoporphyrin compound which includes iron, wherein said at least one modified lactic acid

bacterial cell is obtained by culturing (also referred to herein as "growing") in a medium containing haemin. Applicants submit that the subject matter of claim 13, and claims 14-17 and 29-56 depending therefrom, is enabled through Applicants' teachings of the culturing of lactic acid bacterial cells in a culture medium containing haemin to produce modified lactic acid bacterial cells comprising a protoporphyrin-containing compound, which include iron, at a concentration of at least 0.1 ppm on a dry matter basis.

Similarly, Applicants submit that the subject matter of claim 4, and claims 5-12 depending therefrom, is enabled through Applicants' teachings in the specification. For example, the Office Action expressly acknowledges the enablement of the subject matter of claim 5 directed to the aerobic production of cytochrome d at a concentration of at least 0.1 ppm on a dry matter basis. *See* Office Action, page 4, lines 18-20. Applicants submit that the skilled artisan is enabled to produce modified lactic acid bacterial cells containing at least 0.1 ppm on a dry matter basis of other cytochromes without undue experimentation. This is supported by the declaratory statements of Mr. Asger Geppel, in which Mr. Geppel states that he believes that the invention should work for all types of iron containing porphyrin compounds. *See* paragraph 12 of Geppel Declaration.

Applicants submit that the subject matter of claim 12 is allowable, because the Office Action acknowledges that the specification is enabling for lactic acid bacterial cells modified to reduce LDH activity by at least 10% with treatment under aerobic conditions. *See* Office Action, page 6, lines 1-3.

Applicants submit that the subject matter of claim 16 is allowable because the Office Action acknowledges that the specification is enabling for lactic acid bacterial cells modified to contain at least 0.1 ppm of cytochrome d using mixed lactic acid bacterial strains grown aerobically. *See* Office Action, page 6, lines 10-12.

Applicants submit that the rejection of claims 40-42 is rendered moot by way of the present amendments to the claims.

Claims 48-52 have been amended to recite that the at least one bacterial cell is obtained by culturing in a medium containing 10 mg/L haemin. Applicants submit that the skilled artisan is enabled to make and use the subject matter of claims 48-52 as amended herein without undue experimentation.

Applicants respectfully note that claims 7, 10, 11, 13-15, 34-39, 43 and 44 were indicated as included within the group of claims as rejected under 35 U.S.C. § 112, ¶ 1 paragraph. However, no specific reasoning has been provided in the Office Action stating why these claims are rejected. In the absence of the basis for rejecting these claims, Applicants respectfully request withdrawal of the rejection and an indication of allowance of these claims. Furthermore, Applicants submit that these claims are enabled in light of the declaratory statements of Mr. Asger Geppel. Mr. Asger Geppel considers himself a person of ordinary skill in the technology of lactic acid bacterial cells.

Accordingly, Applicants respectfully request reconsideration and withdrawal of the enablement rejections of claims 4-17, 34-52, and 56 under 35 U.S.C. § 112, 1st paragraph.

Claims Rejections- 35 U.S.C. §103(a)

Claims 4-7, 10-17, 35-39, 43, 44, 48 and 49 were rejected under 35 U.S.C. §103(a) as allegedly unpatentable over "Kaneko *et al.*"

Applicants respectfully disagree and traverse this rejection.

The pending claims are drawn to an *isolated starter culture* useful in manufacturing and preservation of food and feed products comprising at least one modified lactic acid bacterial cell. Applicants respectfully submit that there is no teaching in Kaneko *et al*, nor a suggestion to modify the teachings of Kaneko *et al*, to obtain the claimed *isolated starter culture.*

Applicants submit that the bacterial cultures as described by Kaneko *et al* are used to produce diacetyl and acetoin, but there is no discussion or contemplation of the isolation or harvesting of these bacterial cultures from the end products *following completion of the culturing process* described in Kaneko *et al* for any use, much less as an isolated starter culture. (*See* Kaneko *et al*, Examples 1-5). As a result, not all of the claim elements are taught or suggested by Kaneko *et al*, and Applicants submit that the pending claims are not rendered obvious by the teachings of Kaneko *et al.*

In fact, Kaneko *et al* teach that the culture solution produced in the culturing process, or a concentrate thereof, is used to improve the flavor of food. Kaneko *et al* also suggest that the solution includes diacetyl and acetoin. *See* Kaneko *et al*, column 5, lines 3-10 and Example 1. Furthermore, in each of Examples 1-5, Kaneko *et al* refer to the use of starter cultures for

inoculation, clearly distinguishing the use of bacteria as starter cultures from bacteria remaining at the end of culturing in their own examples. As stated in Applicants' prior response, "starter" culture has a defined or recognized meaning in the art. For example, in the McGraw-Hill Dictionary of Scientific and Technical Terms, 5th Ed., a "starter" in the field of microbiology is defined as "[a] culture of microorganisms, either pure or mixed, used to commence a process, for example, cheese production." *See* McGraw-Hill Dictionary of Scientific and Technical Terms, 5th Ed., definition of Starter [MICROBIO], Sybil Parker Editor in Chief, Copyright 1994. A courtesy copy of this definition was previously provided in Applicants' RCE submission as Appendix C.

Additionally, the concentration of heamin used by Kaneko *et al.* differs signifigantly from the concentration used in Applicants' invention. The molecular weight of haemin is 651 g/mol according to the specification (page 18 lines 23) and Sigma Aldrich (Product # H5533) (a copy of the website is attached-- Exhibit A). Kaneko *et al.* teaches two examples of using haemin in a starter, Example 1 using 5 μM and Example 5 using 1 μM. Kaneko *et al.* also teaches a comparative example using 300 mg/100 mL of haemin, which is a concentration of ~4.6 μM. Id. at Col. 5 lines 15-28. Kaneko *et al.* only includes prophetic discussion of using haemin in a range of 0.1 to 500 μM with a preferred embodiment of 0.5 to 5 μM of heamin. Id. at Col. 3 lines 21-24.

In contrast, the Applicants in their invention use 10 mg/L haemin which is 15 μM, at least three times the amount exemplified by Kaneko *et al.* The reference does not contain any teaching, motivation, or suggestion to increase the amount of haemin from ~ 5 μM to 15 μM. Nor does Kaneko *et al.* teach an isolated starter culture as is required by the claims. Finally, Kaneko *et al.* does not present any evidence that the cultures produced by their method have at least one modified lactic acid bacterial cell comprising at least 0.1 ppm on a dry matter basis of a porphyrin compound which includes iron.

Accordingly, Applicants respectfully request reconsideration and withdrawal of the rejection of claims 1, 4-7, 10-17, 35-39, 43, 44, 48 and 49 under 35 U.S.C. §103(a).

CONCLUSION

An indication of allowance of all claims is respectfully solicited. Early notification of a favorable consideration is respectfully requested. In the event any issues remain, Applicants would appreciate the courtesy of a telephone call to their counsel to resolve such issues and place all claims in condition for allowance.

It is believed that all necessary fees are enclosed. However, if any additional fees are determined to be required, the Commissioner is hereby authorized to charge these fees to the undersigned's **Deposit Account No. 50-0206**.

Respectfully submitted,

HUNTON & WILLIAMS LLP

Date: August 8, 2006

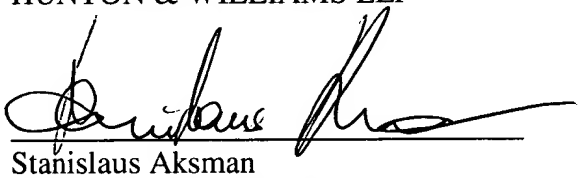
By: 

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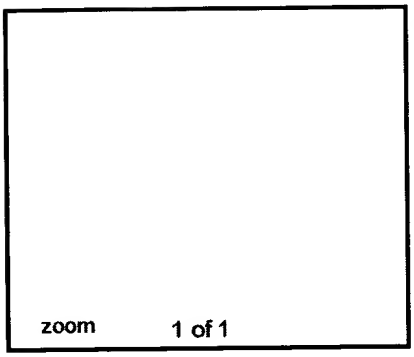
Exhibit A
Sigma Aldrich (Product # H5533)
(downloaded from http://www.sigmaaldrich.com/ on August 8, 2006)

H5533 Hemin

Sigma **from bovine, ≥80%**



Synonym	Chloro(protoporphyrinato)iron(III) Chlorohemin Chloroprotoporphyrin IX iron(III) Ferriprotoporphyrin IX chloride Hemin(chloride)
Molecular Formula	$C_{34}H_{32}ClFeN_4O_4$
Molecular Weight	651.94
CAS Number	16009-13-5
Beilstein Registry Number	5229914
MDL number	MFCD00010726

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H5533

Expand/Collapse All

Price and Availability

Click For Pricing and Availability

Properties

biological source	from bovine
assay	≥80%
storage temp.	2-8°C

References

Reference	Tsutsui, K., Affinity chromatography of heme-binding proteins: Synthesis of hemin-agarose. *Meth. Enzymol.* **123**, 331, (1986)
Merck	*Merck* **13**,4662
Beilstein	*Beil.* **26**,IV,3048

Safety

Safety Statements	22-24/25
WGK Germany	3
F	8

Related Categories

... Plasma Blood Protein > **Plasma, Blood, and Related Proteins and Reagents**

... Metabolites and Cofactors on the Metabolic Pathways Chart > **Porphyrin**

... Serum Proteins and Related Enzymes > **Serum Proteins**